



Azilsartan

Updated: January 13, 2017.

OVERVIEW

Introduction

Azilsartan is an angiotensin II receptor blocker (ARB) used in the therapy of hypertension. It is associated with a low rate of transient serum aminotransferase elevations, but has yet to be linked to instances of acute liver injury.

Background

Azilsartan (ay" sil sar' tan) is an ARB used alone or in combination with other agents for therapy of hypertension. Azilsartan inhibits the renin-angiotensin system by blocking the angiotensin II type 1 receptor (AT1), which prevents the vasoconstriction and volume expansion induced by circulating angiotensin II and which accounts for its antihypertensive activity. Azilsartan was approved for use in the United States in 2011 (the eighth ARB approved for hypertension). Current indications are for treatment of hypertension, either alone or in combination with other antihypertensive agents. Azilsartan is available in 40 and 80 mg tablets under the trade name Edarbi. Fixed combinations of azilsartan (40 mg) with chlorthalidone (12.5 or 25 mg) are also available under the brand name Edarbyclor. The typical dose in adults is 40 to 80 mg once daily, and it is used long term. Side effects are uncommon, but may include headache, dizziness, fatigue, cough, gastrointestinal upset, and fetal toxicity. Several ARBs, but not specifically azilsartan, have been linked to a severe sprue-like enteropathy that typically arises after months or years of therapy and is unresponsive to gluten withdrawal, but resolves promptly with stopping the angiotensin receptor antagonist.

Hepatotoxicity

Azilsartan has been associated with a low rate of serum aminotransferase elevations that, in controlled trials, was no higher than with placebo therapy. These elevations were transient and rarely required dose modification. No specific instances of clinically apparent acute liver injury have been reported in association with azilsartan therapy, but it has been available for a limited time. Other ARBs have been linked to rare instances of symptomatic hepatotoxicity. The onset of liver injury is usually within 1 to 8 weeks of starting therapy and the serum enzyme pattern is typically hepatocellular with an acute hepatitis-like clinical syndrome. In some instances, cholestasis has developed which can be prolonged and relapsing, but ARB therapy has not been associated with vanishing bile duct syndrome or chronic liver injury. Immunoallergic manifestations (rash, fever, eosinophilia) are not common, nor is autoantibody formation.

Likelihood score: E* (Unproved but suspected rare cause of clinically apparent liver injury).

Mechanism of Injury

The cause of the minor serum aminotransferase elevations with azilsartan is not known. Azilsartan is metabolized at least in part by the liver, largely via CYP 2C9, but it has minimal drug-drug interactions.

Outcome and Management

The instances of acute liver injury reported with ARB use have been self-limited and have not resulted in acute liver failure or chronic liver injury. While corticosteroids have been used in cases of severe cholestasis due to ARBs, their efficacy has not been shown and their use is best avoided. Patients with azilsartan induced liver injury should probably avoid use of other ARBs, although cross sensitivity to liver injury among the members of this class of agents has not been shown.

References on the safety and potential hepatotoxicity of azilsartan are given in the Overview section on the Angiotensin II Receptor Antagonists.

Drug Class: [Antihypertensive Agents, Angiotensin II Receptor Antagonists](#)

Other Drugs in the Subclass, Angiotensin II Receptor Antagonists: [Candesartan](#), [Eprosartan](#), [Irbesartan](#), [Losartan](#), [Olmesartan](#), [Telmisartan](#), [Valsartan](#)

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Azilsartan – Edarbi®

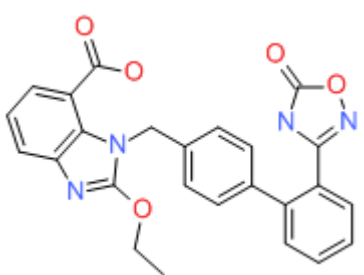
DRUG CLASS

Angiotensin II Receptor Antagonists

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Azilsartan	147403-03-0	C ₂₅ -H ₂₀ -N ₄ -O ₅	 <p>The chemical structure of Azilsartan is shown. It features a central benzimidazole ring system. One nitrogen of the benzimidazole is substituted with an ethoxy group (-OCH₂CH₃). The other nitrogen is substituted with a propyl group (-CH₂CH₂CH₃). The benzimidazole ring is further substituted with a carboxylate group (-COO⁻) and a phenyl ring. The phenyl ring is substituted with a benzimidazole ring, which is in turn substituted with a carboxylate group (-COO⁻) and a nitrogen atom.</p>